

## RISK FACTORS ASSOCIATED WITH HUMAN CYSTIC ECHINOCOCCOSIS IN FLORIDA, URUGUAY: RESULTS OF A MASS SCREENING STUDY USING ULTRASOUND AND SEROLOGY

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**Abstract.** Sonographic evidence of asymptomatic *Echinococcus granulosus* lesions in the liver was found in 156 of 9,515 persons in the Department of Florida, Uruguay. The sensitivity of ELISA and latex agglutination serology compared with ultrasound was 47.6% and 28.1%, respectively, and specificity was > 85%. There was a significant positive association between positive sonography and a personal history of previous but treated *Echinococcus* infection while those that were seropositive but ultrasound-negative were significantly more likely to have a personal history of infection or a history of infection in their family. Prevalence of infection increased significantly with age. There was no correlation between echinococcosis and dog ownership or home slaughter of sheep but offal disposal was important, with an increased prevalence of infection of 3.2%, 2.8%, and 3.1%, respectively, in persons feeding offal to dogs or burying or burning it compared with a prevalence of 0.8–1.5% in those using other methods of disposal. Almost half the population, when questioned, seemed to have sound knowledge about *E. granulosus* and described correct treatment of *E. granulosus* in dogs but this did not affect prevalence. There was a significant positive association between infection and the presence of a fenced fruit/vegetable garden and use of rural waters, particularly the cachimba (a small dam) and the aljibe (a cistern or tank) that collect rainwater from the ground surface and roofs, respectively.

Human cystic echinococcosis (CE) or hydatidosis is acquired by ingestion of eggs of the dog/sheep tapeworm *Echinococcus granulosus* and has its greatest impact on the health of rural residents. Infection can result from close contact with infected dogs through accidental ingestion of eggs from dog feces that contaminate food, soil, and hands. Indirect transfer may occur with carriage of eggs from dog feces to human foodstuffs by house flies and blow flies.<sup>1</sup> The Republic of Uruguay belongs to a group of countries in which *E. granulosus* is endemic. Although a marked reduction in the transmission of *E. granulosus* has been successfully achieved in some countries, this has not occurred in Uruguay. Clinical incidence of CE, based on hospital cases in the period 1962–1974, was 20/100,000 in Uruguay with 53 cases/100,000 in the Department of Florida, Uruguay.<sup>2</sup> In 1993, these figures were 12.4 and 36.1, respectively.<sup>3</sup> Furthermore, between 1984 and 1986, ultrasound examinations of people in four high-risk areas of Uruguay detected asymptomatic *Echinococcus* lesions in 0.7%–2.1%.<sup>4</sup>

Many reports have described the incidence of CE from hospital records and a few provided information from a large number of asymptomatic people,<sup>4–6</sup> but these studies did not statistically evaluate the risk factors that contribute to infection. Sonography is now a reliable, rapid, portable, cheap, and noninvasive method for detecting infection in large numbers of people. Serology also is being increasingly used to determine the prevalence of CE. Thus, to correlate the prevalence of asymptomatic CE with the personal, socioeconomic, and environmental risk factors involved in the transmission of *E. granulosus* to humans in Uruguay, a large sonographic, serologic, and questionnaire survey was used in five localities in the Department of Florida. This department was selected because it was representative of the rest of the country in terms of farming, social, and geographic conditions. The study was part of a framework to produce baseline data on which to determine options for control of

*E. granulosus* in this country. Recently in the same survey area, *E. granulosus* was shown to be endemic in sheep and dogs.<sup>7,8</sup> Prevalences were 67.4% in sheep 4.5 years of age and older and 13.2% in rural dogs with reinfection of dogs occurring rapidly at between two and four months after treatment.

### POPULATION AND METHODS

**Study area.** The Department of Florida was chosen as the survey area because it was representative of the farming, socioeconomic, and geographic aspects common throughout Uruguay. The Department encompasses 10,500 km<sup>2</sup> and the population of 66,500 has a rural:urban residence ratio of 1:3. With the exception of the capital of Florida, the majority of urban residents live in small villages or towns, each with a population of < 3,000. The topography is < 200 m above sea level and primarily prairie (savannah) land. The economy is primarily rural agriculture based on sheep meat, wool, and cattle, mainly for beef. An average of 2–4 dogs, but as many as 8–10, live on each farm. The majority are working dogs and none are confined.<sup>8</sup> There is an average of 1–1.5 dogs per household in the rural villages and towns.

**Sonography.** The sonographic equipment used was a portable, linear, convex, sector ultrasound scanner (Echo Camera Model SSD-500, 3.5 MHz; Aloka, Tokyo, Japan). From May 1993 to July 1994, people were encouraged by local radio, newspapers, and leaflets to attend survey clinics, many of which were held in village and rural schools. The project was approved by the Ethical Committee of the School of Medicine, Universidad de la Republica. The participants were volunteers. The procedures were explained to the participants and consent was obtained verbally at the time the participants answered the supervised questionnaire that started the examination process. In the case of school children, administrative consent was obtained by the Ministry of Ed-

ucation and parental consent was obtained for each child examined. Thoracic radiography with a portable miniature machine was carried out on the first 1,000 persons examined in Nico Perez/Battle y Ordonez, but this was then discontinued because thoracic radiography revealed an additional prevalence of only 0.2%.

Parenchymal liver sonographic images were classified into 11 types considered to be of *Echinococcus* origin or were diagnosed as simple hepatic cysts. The latter have a prevalence of approximately 2.5%, are apparently derived from congenitally aberrant bile duct epithelium, and are normally asymptomatic.<sup>9</sup> The *Echinococcus* lesions have been previously described by Perdomo and others.<sup>10</sup> Types were defined and separated based on their sonographic image and clinical history. Validation of the diagnosis of CE was achieved in 60 patients who opted for treatment (some for cholelithiasis) by surgery, or puncture, aspiration, introduction of protoscolicide, and re-aspiration, or puncture and aspiration. Briefly, the following are the sonographic images and their definitions: type 1 = hyaline *Echinococcus* cyst (rounded, anechoic space circumscribed by a defined and regular wall and with posterior reinforcement); 2 = cyst with a snow-like sand sign (small dense and mobile echoes from moving brood capsules and protoscoleces); 3 = cyst with a tram sign (double membrane margin in some areas); 4 = cyst with a water lily sign (undulating, detached and floating membranes); 5 = multivesicular with daughter vesicles; 6 = some daughter vesicles but much of the cyst cavity replaced by solid echogenic material; 7 = a solid heterogeneous echo pattern with a rolled parasite membrane recognizable; 8 = a solid heterogeneous echo pattern; 9 = a solid homogeneous echo pattern; 10 = a small, fully calcified lesion; and 11 = a hyperechoic, calcified arch with an acoustic shadow and unknown contents. The simple, nonparasitic, hepatic cyst was an anechoic space without a defined wall. For some serologic analyses, types were grouped as group I = definite *Echinococcus* cyst (types 2–7); group II = pathologic sequel to *Echinococcus* cyst (types 8–11); group III = hyaline *Echinococcus* cyst; and group IV = nonparasitic, simple, hepatic cyst. Groups I, II, and III were combined as definite CE cases for all other analyses. The type 1 hyaline *Echinococcus* cyst and the simple hepatic cyst were differentiated by their sonographic appearance and clinical history.<sup>10</sup>

**Serology.** For each positive sonographic case, a sex- and age-matched case-control from the same district but with negative sonography was sampled. Additional negative controls were sera collected from each case that presented abdominal pathology, i.e., simple cyst, cholelithiasis, renal cyst, tumor, etc. Samples were examined by ELISA and latex agglutination (LA). Positive and negative control sera for the tests were pooled from surgically confirmed CE patients and from healthy persons, respectively, living in the region of the survey.

The ELISA was carried out using microtiter plates (Sumilon, Tokyo, Japan) coated with 100  $\mu$ l of fertile bovine *Echinococcus* cyst fluid (from liver and lungs) collected and semi-purified according to the method of Marco and Nieto,<sup>11</sup> and used at a final protein concentration of 20  $\mu$ g/ml. One hundred microliters of test sera (1:50 dilution) were added to each well. Anti-*Echinococcus* antibodies were detected with horseradish peroxidase in citrate phosphate buffer.<sup>12</sup>

Optical density (OD) values were read in an ELISA plate reader (Sigma Diagnostics, St. Louis, MO) at 405 nm. Latex agglutination was carried out according to the method of Barbierri and others<sup>13</sup> using the commercial diagnostic kit produced by LBTEX (Montevideo, Uruguay). The negative cut-off point was the mean + 3 SD of the OD values of negative sera from the population under study.

**Personal, sociologic, and environmental parameters.** A number of questions were prepared. A questionnaire was filled out by trained personnel, e.g., teachers, nurses, and medical students, who talked to each person surveyed.

**Statistical analyses.** Confidence intervals were estimated using the arc-sin approximation of the binomial distribution. The relationships between positive and negative sonography and the various personal, socioeconomic, and environmental factors were made using the chi-square test, as were those between positive sonography and the serologic results obtained by ELISA and LA. The ELISA and LA results were then compared with the categories of lesions in groups I–IV using the Kolmogorov-Smirnov test, and determination as to whether the differences were due to a location change was made with the Mann-Whitney test. A test for the comparison of binomial distributions was based on the arc-sin approximation. All these tests are from Silvey<sup>14</sup> and Gibbons.<sup>15</sup>

## RESULTS

**Sonography.** A total of 9,515 persons presented themselves for examination. Ultrasound examinations detected 156 cases of asymptomatic CE; 1.6% or 1,640/100,000 of the population in the area surveyed (upper 95% confidence interval [CI] = 3.46%) had lesions compatible with *E. granulosus* infection. Of the 156 cases, 62 (0.7%) had recognizable *Echinococcus* lesions (group I, types 2–7), 23 (0.2%) showed the pathologic sequelae of *Echinococcus* cysts (group II, types 8–11), and 71 (0.7%) had hyaline *Echinococcus* cysts (group III, type 1). An additional 44 persons (0.5%) were classified as having nonparasitic, simple hepatic cysts. The upper 95% CIs for these lesions were group I = 2.18%, group II = 1.34%, group III = 2.33%, and simple hepatic cysts = 1.84%. Three patients had an *Echinococcus* lesion plus a simple, hepatic cyst but were included with the *Echinococcus* groups. Ninety-six percent of the *Echinococcus* lesions were in the liver, but two were in the peritoneal cavity and one each in the kidney, spleen, pancreas, and psoas muscle. Since thoracic radiography of the first 1,000 persons revealed only an additional two cases, this procedure was discontinued. The 95% CI of any person being negative for a cyst or lesion was 97.2–98.1%.

**Personal, sociologic, and environmental parameters.** Asymptomatic cases occurred in persons of all ages, but age group analysis showed that there was a statistically significant increase in CE with age ( $P = 0.0001$ ) (Table 1). Prevalence increased from 0.41% in the 0–9 years of age group to 6.15% in the  $\geq 80$  years of age group.

All other relationships are summarized in Table 2. The vast majority (98.4%) of persons surveyed were negative for CE by ultrasound. Despite this, a personal history of CE given by 2.3% (212 persons) of the population surveyed significantly increased ( $P = 0.00003$ ) the likelihood of a person having an asymptomatic infection, with 10.8% of these cur-

TABLE 1

Age distribution of asymptomatic cystic echinococcus in humans in the Department of Florida, Uruguay

Age (years)	Total no. examined	No. positive	Prevalence
0-9	1,719	7	0.41%
10-19	1,898	13	0.68%
20-29	1,028	12	1.17%
30-39	1,268	18	1.42%
40-49	1,230	26	2.11%
50-59	913	26	2.85%
60-69	822	27	3.28%
70-79	473	19	4.02%
≥80	130	8	6.15%
Total	9,481	156	

rently positive for an *Echinococcus* lesion. In contrast, a family history of CE did not increase the likelihood of asymptomatic infection. More than 40% of those surveyed seemed to have a good understanding of CE, and most dog owners (60.9%) seemed to know about the correct use of praziquantel for treatment of their dogs, but levels of knowledge had little influence on the prevalence of CE.

Dog owners made up 59.1% of the population because a few farms and a higher proportion of households in villages and towns did not own any dogs and workers on farms often were not dog owners. It was the type of food fed to the dogs that significantly altered prevalence of CE among these owners ( $P = 0.045$ ). Thus, some owners, albeit a small number (6.5%), still fed raw viscera to their dogs and this significantly increased prevalence of CE among these owners to 3.1%. The method for disposal of offal from home-slaughtered animals (mainly sheep) did have a significant effect on the prevalence of *Echinococcus* in humans ( $P = 0.0049$ ). The prevalence of *Echinococcus* was higher (3.2%) among those who fed viscera to dogs, as well as in those who buried (3.1%) or burned (2.8%) the offal, compared with a prevalence of only 1.5% among those who fed the offal to pigs and of 0.8% if the offal was cooked or discarded (more detailed information on the exact method of disposal could not be obtained).

Having a vegetable/fruit garden did not affect prevalence, but when infection in those who gardened in an enclosed area (2.2% infected) was compared with the others (1.5% infected) it was significantly higher ( $P = 0.042$ ). The type of water used by a household also significantly influenced the prevalence of infection ( $P = 0.0107$ ). The greatest prevalence of *Echinococcus* was present in those who drank water from a cachimba (a small dam that collected rainwater from the ground surface) (3.3%) and from an aljibe (a cistern or tank that collected rainwater from the roof of the house) (2.9%). Those persons who drank water that was collected locally for the individual household were no more likely to boil their water than those drinking commercially obtained water. Thus, only 23.6% of those who drank water from an arroyo (small stream), 30.7% from a cachimba, 25.1% from a pozo (a well or borehole), and 34.5% from an aljibe boiled their water compared with 38% who drank commercially treated, piped water.

**Serology.** Eight hundred thirty-one and 856 samples were tested by ELISA and LA, respectively (Table 3). For the

ELISA, 147 samples were from CE-positive patients and an equal number were from sex- and age-matched controls. For the LA, these numbers were 146 samples for each group. The additional samples tested were from patients with non-CE abdominal pathology. There was a good correlation between positive ELISA or LA results and positive sonography ( $P = 0.00001$ ). Serology did not discriminate between infections with different lesions types (groups I, II, or III) ( $P = 0.40$ , by Kolmogorov-Smirnov test and  $P = 0.2105$ , by the Mann-Whitney test). Sensitivities for the ELISA and LA were 47.6% and 28.1%, respectively, and the specificity of each test was 88.4% and 85.5%, respectively. The history of the samples that were seropositive but were negative by sonography was examined further. Among those that were LA seropositive and ultrasound negative, 1.93% and 16.98%, respectively, had a familial or personal history of CE compared with 0.69% and 0.57% that were seropositive and ultrasound negative but without such a history of CE. For the ELISA, these figures were 0.02% and 14.62% compared with 0.007% and 0.007%, respectively. Thus, persons positive by one or both of these serologic tests, even though ultrasound negative, were significantly more likely to have a familial ( $P = 0.007$ ) or personal ( $P = 0.000001$ ) history of *Echinococcus* infection. The location of a previous *Echinococcus* cyst(s) (liver, lung, other, or multiple) did not influence the results ( $P = 0.215$ ).

#### DISCUSSION

The prevalence of asymptomatic cystic echinococcosis in the Department of Florida, Uruguay was relatively high. The 156 (1.6%) of 9,515 persons positive for an asymptomatic, hepatic *E. granulosus* lesion by abdominal sonography is similar to that of other recent sonographic studies in Uruguay. Perdomo and others<sup>4</sup> reported infection in 1.4% of 6,027 people examined in four Departments, and Paolillo and others<sup>16</sup> found a prevalence of 1.3% in 376 students in Sarendi del Yi. The present result is an underestimate since an additional two persons (0.2%) of the 1,000 tested by thoracic radiography had lung *Echinococcus* lesions. However, the underestimation is considered slight because Perdomo and others<sup>4</sup> failed to detect any lung cysts in 3,593 people examined radiologically, while Purriel and others<sup>2</sup> reported an average lung prevalence of 0.3% from records of radiology clinics in hospitals from 1948 to 1964. All of the above surveys demonstrate a low prevalence of lung cysts in asymptomatic patients. In contrast, hospital surveys that reflect *E. granulosus* infection in patients presenting with clinical symptoms reported that 15–25% of cysts are in the lungs, 10–15% are found in other organs, and 60–80% of the cysts are in the liver.<sup>17–19</sup> This difference between population prevalence (asymptomatic) and hospital prevalence (clinical cases) must indicate that cysts in organs other than the liver are more likely to provoke clinical symptoms, thus initiating diagnosis. Also, the number of asymptomatic lesions detected in this study was considerably greater than the annual incidence of surgical cases in persons originating from the same Department of Florida. Morelli and others<sup>3</sup> and J. Monti and C. Carmona (unpublished data) in 1988–1993 reported an average hospital incidence of 22–24/100,000. Thus, assuming there is no rapid change in prev-

TABLE 2

Percentage of people in the Department of Florida, Uruguay with asymptomatic cystic echinococcosis (CE) detected by sonography in relation to various personal, socioeconomic, and environmental factors

Factor		Number in category	% infected with <i>Echinococcus</i>	Chi-square <i>P</i> values	Association
Male		4,431	1.6	0.9761	No
Female		5,079	1.7		
Personal history of CE	Yes	212	10.8	0.00003	Yes
	No	9,188	1.4		
Family history of CE	Yes	1,964	1.9	0.28897	No
	No	7,431	1.6		
Knowledge concerning <i>Echinococcus</i>					
Sufficient		3,970	1.9	0.092	Moderate
Some		2,566	1.6		
Insufficient		2,829	1.2		
Dog owner					
Yes		5,562	1.7	0.9783	No
No		3,843	1.7		
Food given to dogs					
Raw viscera		354	3.1	0.045	Yes
Cooked viscera		1,338	2.2		
Raw meat		770	1.0		
Table scraps		3,045	1.4		
Praziquantel					
Used correctly		3,330	2.0	0.2396	No
Used incorrectly		783	2.0		
Not used		453	0.7		
Home slaughter					
In enclosure		1,367	1.8	0.21563	No
Without enclosure		1,162	2.2		
None		6,867	1.5		
Offal disposal					
Fed to dogs		759	3.2	0.0049	Yes
Fed to pigs		586	1.5		
Discarded		394	0.8		
Buried		145	2.8		
Cooked		472	0.8		
Burnt		135	3.1		
Vegetable garden					
Enclosed		2,083	2.2	0.2106	No
Not enclosed		1,639	1.5	(Enclosed garden versus others	Yes
None		5,680	1.5	<i>P</i> = 0.042)	
Water origin					
Arroyo		55	1.8	0.0107	Yes
Cachimba		215	3.3		
Pozo		1,180	1.5		
Aljibe		1,009	2.9		
Commercial piped		6,917	1.4		
Water					
Boiled		2,616	1.7	0.8858	No
Not boiled		6,601	1.6		

alence or acquisition of CE and that other diseases and factors are relatively stable, the conversion rate of asymptomatic to clinical CE is 0.0134.

The specificity of sonography when confirmed surgically was 83–94% in three studies.<sup>17, 20</sup> In the present series of patients, specificity has been calculated as 92–94% based on 51 patients with *E. granulosus* lesions and nine patients with simple hepatic cysts confirmed surgically.<sup>10</sup> Sensitivity can only be estimated for two reasons. Early lesions up to per-

haps one year after infection will not be detected. This is because the limit of detection of sonography is a lesion, unless calcified, of approximately 1.5 cm, and early growth of *Echinococcus* cysts has been reported as approximately 0.5–1.5 cm/year.<sup>18</sup> Also, both obese and thin persons are known to create a practical problem that limits the sensitivity of ultrasound. Although the impact of the latter cannot be estimated, the numbers of early cysts not detected can be calculated from the incidence rate of infection. The data gath-



TABLE 3

Correlation between sonography and serology in detection of cystic echinococcosis in humans

Echography result	ELISA*			LA†		
	Positive	Negative	Total	Positive	Negative	Total
Positive	70	77	147	41	105	146
Negative	98	586	684	89	621	710
Total	168	663	831	130	726	856

\* Enzyme-linked immunosorbent assay.

† Latex agglutination.

ered in this survey give a yearly incidence rate of 53/100,000 or 46/100,000. The former value was calculated by the equation, prevalence (1.6%) = incidence  $\times$  duration, where duration has been taken as an average of 30 years (although infection for up to 53 years has been documented).<sup>21</sup> The latter value, estimated by the average yearly increase in prevalence in those up to 70–79 years of age (Table 1) and assuming that no lesions became undetectable but considering the population composition (census data), was in close agreement. Assuming these 46–53 new cases a year will not be detected by ultrasound for an estimated 1–1.5 years, the sensitivity is estimated to be 95–96%.

The sensitivity of serology was low (28–48%), particularly that of the LA test, when compared with sonography (92–94%). This confirms that it is essential to calculate predictive values before a test is used extensively. Macpherson and others<sup>22</sup> also reported a low sensitivity (27%) of an ELISA in Turkana, Kenya, although Bchir and others<sup>23</sup> described 99% sensitivity for an ELISA confirmed by counter-immunoelectrophoresis in Tunisia. Several recent studies reported improved sensitivity using purified antigens and specific IgG responses.<sup>24, 25</sup> Specificity of the ELISA and LA tests in this study was good (> 85%). Furthermore, some of the patients who were ultrasound negative and yet seropositive could reflect infection in organs other than the abdomen, while the significant correlation between positive serology and a personal and/or familial history of CE could reflect persistence of antibody after treatment, recrudescence of infection after surgery, or reinfection when the patient returned to the same unaltered environment. In other studies, postoperative recurrence rates have been as high as 2–22%.<sup>26</sup>

Several personal, socioeconomic, and environmental factors correlated with an increased prevalence of asymptomatic CE. Prevalence increased with age, indicating that the infection pressure must be low such that protective immunity does not develop in the human population. A low infection pressure also has been demonstrated for sheep in the survey area.<sup>7</sup> A personal history, but not a family history of CE, increased the likelihood of infection. This correlation might reflect an individual susceptibility, perhaps genetic or through poor personal hygiene, and/or continued exposure to environmental contamination (directly or via flies), although reactivation of a previous infection cannot be ruled out.

Dogs are infected with *E. granulosus* by eating sheep viscera. Thus, although home slaughter of animals was not significantly related to infection, feeding the offal to dogs significantly increased the prevalence of CE in these dog owners. The results also suggested that dogs may have access to

viscera that is burned or buried. Despite this, in this study there was no significant association between dog ownership and CE unless the owners fed offal to their dogs. This is in contrast to Paolillo and others,<sup>16</sup> who reported higher prevalence in students owning infected dogs, but in a sample too small for analysis. Several investigators have suggested that close contact with dogs could explain high levels of CE.<sup>6</sup> A major factor in the lack of an association between dog ownership and CE might be that a high proportion (60.5%) of dog owners understood the correct use of praziquantel. The lack of an association between infection and dog ownership also might be because many dogs can roam freely to contaminate the soil. Furthermore, eggs of *Taenia hydatigena* and *E. granulosus* can be transmitted in high numbers from dog feces by flies over a distance of 80 m, and a few eggs may be dispersed in flies over a distance of 10 km to contaminate areas distant from the dog.<sup>1</sup>

Flies appear not to be the most important source of contamination for home-grown fruits and vegetables because fenced gardens, not just the presence of a vegetable garden, were associated with increased levels of CE. Many houses have a fence or wall surrounding the area in which vegetables may be grown and into which dogs frequently can be allowed loose.

There was a significant correlation between *Echinococcus* infection and some types of rural waters. Of the rural water types, water from a cachimba or an aljibe seemed to have the most influence on CE. A cachimba is a natural depression (small dam) in the terrain into which surface rainwater drains. Rainwater draining into a cachimba could collect eggs from infected dog feces. Also, flies are known to contaminate soil and vegetation<sup>1</sup> and could do so in the water catchment area. An aljibe is an artificially built (usually brick or cement) cistern or tank often 2  $\times$  2 m but up to 5  $\times$  10 m. The aljibe is usually built underground and situated in a house courtyard (Figure 1) or near the house. Rainwater from the house roof is frequently piped into the aljibe so that eggs in feces deposited by flies on the roof (or by dead flies themselves in the gutters, etc.), may be washed into the tank. Surface or subterranean water can seep through the porous walls of some tanks. In contrast, a pozo is an artificially dug well approximately 1.5 m in diameter and up to 30–50 m deep, usually dug a greater distance from the house, used for collecting subterranean water (which did not correlate with infection). Twenty percent are machine-bored holes a few inches in diameter from which water is extracted by another machine. These are much less likely to collect eggs or flies.

The results show that intervention in the form of education about the life cycle of *E. granulosus* and the treatment and correct feeding of dogs is important for the control of CE. While the proportion of the population drinking from local farm water sources has decreased from 41% in 1984–1986<sup>4</sup> to 26% currently, these waters are likely to be drunk unboiled. Water should be boiled for drinking and washing fruits and vegetables. In particular, dogs should be excluded from gardens and, if possible, from the catchment areas for rainwater supplying the cachimba and aljibe, although it may be difficult to prevent contamination of these by flies. Dogs should not be fed raw viscera. Since questionnaire answers are often unreliable, continued education must ensure that



FIGURE 1. An aljibe in a courtyard of a house in Florida, Uruguay. The walled surroundings of the opening of the cistern lying underground are visible. The opening is usually covered. Water is taken by bucket and pulley. An important source of water for the cistern is rainwater from the house roof piped into the cistern.

dog owners really do understand the correct praziquantel dosage regimen.

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#### REFERENCES

1. Lawson JR, Gemmell MA, 1990. Transmission of taeniid tapeworm eggs via blowflies to intermediate hosts. *Parasitology* 100: 143–146.
2. Purriel P, Schantz PM, Beovide H, Mendoza G, 1974. Human echinococcosis (hydatidosis) in Uruguay: a comparison of indices of morbidity and mortality, 1962–1971. *Bull World Health Organ* 49: 395–402.
3. Morelli A, Maurin L, Agulla J, Sambran Y, Islas W, Sapia M, Vignolo J, 1994. *Hydatidosis in Uruguay. National Surgical Prevalence, 1993*. Montevideo, Uruguay: Comision Nacional Honoraria de Lucha Contra la Hidatidosis, Tradinco, S.A.
4. Perdomo R, Parada R, Alvarez C, Cattivelli D, Geninazzi H, Barrague AD, Ferreira C, Rivero E, Monti J, Parada J, 1990. Estudio epidemiologico de hidatidosis. Deteccion precoz por ultrasonido en areas de alto riesgo. *Rev Med Uruguay* 6: 34–47.
5. Macpherson CNL, Spoerry A, Zeyhle E, Romig T, Gorfe M, 1989. Pastoralists and hydatid disease: an ultra-sound scanning prevalence survey in East Africa. *Trans R Soc Trop Med Hyg* 84: 243–247.
6. Schantz, PM, Chai J, Craig PS, Eckert J, Jenkins DJ, Macpherson CNL, Thakur A, 1995. Epidemiology and control of hydatid disease. Thompson RCA, Lymbery AJ, eds. *Echinococcus and Hydatid Disease*. Wallingford, United Kingdom: CAB International, 233–331.
7. Cabrera PA, Haran G, Benavidez U, Valledor S, Perera G, Lloyd S, Gemmell MA, Baraibar M, Morana A, Maissonave J, Carballo M, 1995. Transmission dynamics of *Echinococcus granulosus*, *Taenia hydatigena* and *Taenia ovis* in sheep in Uruguay. *Int J Parasitol* 25: 807–813.
8. Cabrera PA, Parietti S, Haran G, Benavidez U, Lloyd S, Perera G, Valledor S, Gemmell MA, Botto T, 1996. Rates of reinfection with *Echinococcus granulosus*, *Taenia hydatigena*, *Taenia ovis* and other cestodes in a rural dog population in Uruguay. *Int J Parasitol* 26: 79–83.
9. Marn CS, Bree RL, Silver TM, 1991. Ultrasonography of the liver. Technique and focal and diffuse disease. *Radiol Clin North Am* 29: 1151–1170.
10. Perdomo R, Alvarez C, Monti J, Ferreira C, Chiesa A, Carbo A, Alvez R, Grauert R, Stern D, Carmona C, Yarzabal L, 1997. Principles of the surgical approach in human liver cystic echinococcosis. *Acta Trop* 64: 109–122.
11. Marco M, Nieto A, 1991. Metalloproteinases in the larvae of *Echinococcus granulosus*. *Int J Parasitol* 21: 743–746.
12. Matsuda H, Tanaka H, Blas F, Nosenas J, Tokawa T, Ohsawa S, 1984. Evaluation of ELISA with ABTS, 2-2'-azino-bis-(3-ethylbenzthiazoline sulfonic acid) as the substrate of peroxidase and its application to the diagnosis of schistosomiasis. *Jpn J Exp Med* 54: 131–138.
13. Barbierri M, Sterla S, Battistoni J, Nieto A, 1993. High performance latex reagent for hydatid serology using an *Echinococcus granulosus* lipoprotein antigen fraction purified from cyst fluid in one step. *Int J Parasitol* 23: 565–572.
14. Silvey SD, 1970. *Statistical Inference*. London: Chapman Hall.
15. Gibbons JD, 1985. *Nonparametric Statistical Inference*. Second edition. New York: Marcel Dekker, 122–170.
16. Paolillo E, Botto B, Cohen H, Dibarboure L, Rodriguez L, Antoniello L, Rios F, Dibarboure H, 1991. Hidatidosis: un problema de atencion primaria en salud. *Rev Med Uruguay* 7: 32–37.
17. Amman R, Eckert J, 1995. Clinical diagnosis and treatment of echinococcosis in humans. Thompson RCA, Lymbery AJ, eds. *Echinococcus and Hydatid Disease*. Wallingford, United Kingdom: CAB International, 411–463.
18. Grove DI, Warren KS, Mahmoud AF, 1976. Algorithms in the diagnosis and management of exotic diseases: echinococcosis. *J Infect Dis* 133: 354–358.

19. El Idrissi AL, Mahjour J, Ayoujil M, Barkia A, 1997. Retrospective survey for surgical cases of cystic echinococcosis in Morocco (1980–1992). Anderson FL, Ouhelli H, Kachani M, eds. *Compendium on Cystic Echinococcosis in Africa and in Middle Eastern Countries with Special Reference to Morocco*. Provo, UT: Brigham Young University Press, 194–203.
20. El-Tahir MI, Omojola MF, Malatania T, Al-Saigh AH, Oginbiyi OA, 1992. Hydatid disease of the liver: evaluation of ultrasound and computed tomography. *Br J Radiol* 65: 390–392.
21. Pawlowski ZS, 1997. Critical points in the clinical management of cystic echinococcosis: a revised review. Anderson FL, Ouhelli H, Kachani M, eds. *Compendium on Cystic Echinococcosis in Africa and in Middle Eastern Countries with Special Reference to Morocco*. Provo, UT: Brigham Young University Press, 119–135.
22. Macpherson CNL, Romig T, Zeyhle E, Rees PH, Were JBO, 1987. Portable ultrasound scanner versus serology in screening for hydatid cysts in a nomadic population. *Lancet* 2: 259–261.
23. Bchir A, Larouze B, Soltani M, Hamdi A, Bouhaouaia H, Dcuic S, Bouden L, Ganouni A, Achour H, Gaudebout C, 1991. Echotomographic and serological population-based study of hydatidosis in central Tunisia. *Acta Trop* 49: 149–153.
24. Aceti A, Pennica A, Teggi A, Fondacaro LM, Caferro M, Leri O, Tacchi G, Celestino D, Quaranta G, de Rosa F, Sebastiani A, 1994. IgG subclasses in human hydatid disease: prominence of the IgG4 response. *Int Arch Allergy Appl Immunol* 102: 347–351.
25. Wen H, Craig PS, 1994. Immunoglobulin-G subclasses in human cystic and alveolar echinococcosis. *Am J Trop Med Hyg* 55: 741–748.
26. Morris DL, Richards KS, 1992. *Hydatid Disease: Current Medical and Surgical Management*. Oxford: Butterworth-Heinemann.